Chronic myeloid leukemia stem cell biology.

Journal: Curr Hematol Malig Rep

Publication Year: 2012

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PubMed link: 22467334

Funding Grants: Derivation and Characterization of Myeloproliferative Disorder Stem Cells from Human ES Cells, Derivation and Characterization of Cancer Stem Cells from Human ES Cells, Preclinical development of a pan Bcl2 inhibitor for cancer stem cell directed therapy

Public Summary:
Leukemia progression and relapse is fueled by leukemia stem cells (LSC) that are resistant to current treatments. In the progression of chronic myeloid leukemia (CML), blast crisis progenitors are capable of adopting more primitive but deregulated stem cell features with acquired resistance to targeted therapies. This in turn promotes LSC behavior characterized by aberrant self-renewal, differentiation, and survival capacity. Multiple reports suggest that cell cycle alterations, activation of critical signaling pathways, aberrant microenvironmental cues from the hematopoietic niche, and aberrant epigenetic events and deregulation of RNA processing may facilitate the enhanced survival and malignant transformation of CML progenitors. Here we review the molecular evolution of CML LSC that promotes CML progression and relapse. Recent advances in these areas have identified novel targets that represent important avenues for future therapeutic approaches aimed at selectively eradicating the LSC population while sparing normal hematopoietic progenitors in patients suffering from chronic myeloid malignancies.

Scientific Abstract:
Leukemia progression and relapse is fueled by leukemia stem cells (LSC) that are resistant to current treatments. In the progression of chronic myeloid leukemia (CML), blast crisis progenitors are capable of adopting more primitive but deregulated stem cell features with acquired resistance to targeted therapies. This in turn promotes LSC behavior characterized by aberrant self-renewal, differentiation, and survival capacity. Multiple reports suggest that cell cycle alterations, activation of critical signaling pathways, aberrant microenvironmental cues from the hematopoietic niche, and aberrant epigenetic events and deregulation of RNA processing may facilitate the enhanced survival and malignant transformation of CML progenitors. Here we review the molecular evolution of CML LSC that promotes CML progression and relapse. Recent advances in these areas have identified novel targets that represent important avenues for future therapeutic approaches aimed at selectively eradicating the LSC population while sparing normal hematopoietic progenitors in patients suffering from chronic myeloid malignancies.